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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,646	02/22/2002	Robert Norman Rice	37921-2	1954

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EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,646	RICE ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,7,10-16,18-21,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,7,10-16,18-21,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 1, 2, 6, 7, 10-13, 15, 16, 18-21, 30, and 31 are rejected under 35 U.S.C. 102(a) as being anticipated by Patrone et al. (*BioTechniques*, Vol. 29, No. 5).

3. For purposes of examination, the phrase "one or more internal or external stimuli" has been interpreted as encompassing aging, and as such, the processing of two samples, dilution, or duplicates at different times fairly encompasses two portions of cells that are of different ages.

4. For purposes of examination, the phrase "at least a portion," as well as the phrase "an exogenous transgene" is considered to fairly encompass any portion or segment of said gene, including that of a single nucleotide that could also be found in any other sequence, including those normally found in the cell's RNA.

5. For purposes of examination, the act of "quantifying" as well as "quantifiable nascent RNA transcripts" are each considered to encompass both direct and indirect means of quantification.

6. Patrone et al., teach at length performing a nuclear run-on assay where nuclei are isolated from human (applicant's mammalian) cells (page 1014, left column), and are further treated such that transcription of nascent RNA is achieved, and in so doing biotin-16-UTP is incorporated

into said RNA (page 1014. left column). The biotinylated RNA is then absorbed onto a resin as a result of the label. The RNA is quantified by means of conducting PCR and quantifying the amplicons (page 1012, abstract; page 1014, bridging to 1015). Such indirect means of quantification are encompassed by the claims (*supra*).

7. In view of the above remarks, and in the absence of convincing evidence to the contrary, claims 1, 2, 6, 7, 10-13, 15, 16, 18-21, 30, and 31 are rejected under 35 U.S.C. 102(a) as being anticipated by Patrone et al. (*BioTechniques*, Vol. 29, No. 5).

Claim Rejections - 35 USC § 103

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 2, 6, 7, 10-16, 18-21, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava et al. (*Methods in Molecular Biology*, 1998, Vol. 86, 201-207) in view of applicant's admissions, and US Patent 5,945,522 (Cohen et al.).

11. Srivastava et al., teach at length of conducting nuclear run-off assays wherein nuclei from cells are isolated from prokaryotic cells (page 203), and nascent RNA is elongated (page 204) where labeled UTP is incorporated into the nascent RNA. RNA elongation is stopped prior to quantification. As seen at page 204, bridging to page 205, the mRNA is then quantified as a result of it hybridizing to cDNA fragment (page 204, bridging to page 205).

12. While Srivastava et al., does teach using labeled ribonucleotides, they do not teach using biotin-labeled ribonucleotides, nor do they teach isolating the labeled RNA through the label, nor that the nuclei are from mammalian cells

13. Cohen et al., column 35, last paragraph, teach incorporating biotin-16-UTP into nascent RNA from human cancer cell nuclei, that the biotinylated RNA is then isolated through the label and is subsequently quantified.

14. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modified the procedure of Srivastava et al., by incorporating biotin-16-UTP into the nascent RNA as such would have allowed for the ready isolation of RNA through the label and to not risk the safety issues surrounding the storage and handling of radioactive nucleotides. In view of the detailed teachings of the prior art, and of applicant's admission at page 12 of their response of 04 June 2004 that "[o]ne skilled in the art is well aware of numerous methods of quantifying nascent RNA transcripts," the ordinary artisan would have been both amply motivated and would have had a most reasonable expectation of success.

To the extent that the claims recite specific means of handling, such methodologies are considered to be the product of routine optimization and do not constitute a patentable difference. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

15. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1, 2, 6, 7, 10-16, 18-21, 30, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava et al. (*Methods in Molecular Biology*, 1998, Vol. 86, 201-207) in view of applicant's admissions, and US Patent 5,945,522 (Cohen et al.).

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

17. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

19. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
28 July 2004